Laryngoscope
Investigative Otolaryngology

ORIGINAL RESEARCH OPEN ACCESS

Pollen Exposure and Chronic Rhinosinusitis Quality of Life Disease Severity

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Received: 7 August 2025 | **Revised:** 8 October 2025 | **Accepted:** 5 November 2025

Funding: Grant support for this investigation provided through the National Institute on Deafness and Other Communication Disorders (R01 DC005805) (Co-Principal Investigators: T.L.S. and Z.M.S.) for T.L.S., J.C.M., J.A.A., V.R.R., and Z.M.S. The funding organization played no role in the design or conduct of this study, or the preparation, review, approval, or decision to submit this manuscript for publication.

Keywords: chronic rhinosinusitis | endoscopic sinus surgery | environment | multi-institution | particulate matter | pollen | preoperative exposure | quality of life | SNOT-22 | surgical outcomes

ABSTRACT

Background: Environmental factors, such as air irritants, may play an important role in chronic rhinosinusitis (CRS); however, no studies to date have examined the role of pollen in CRS disease severity. Here, we analyze the effects of pollen exposure on disease-specific and general quality-of-life (QOL) reports.

Methods: Patients were enrolled prospectively across four academic medical centers and completed the 22-item SinoNasal Outcome Test (SNOT-22) and Medical Outcomes Study Questionnaire Short-Form 6-D (SF-6D) surveys at enrollment. Mean annual pollen exposure over a 5-year period before enrollment was obtained from the National Allergy Bureau using residence zip codes. Unadjusted Spearman's correlation coefficients (r_s) and 95% confidence intervals (CI) were calculated.

Results: One hundred and three patients were included and 55% had a history of allergy. Higher 5-year mean ragweed pollen exposure correlated with worse presenting SNOT-22 ($r_s = 0.24$; 95% CI: 0.033, 0.42; $p = 0.019$) and SF-6D scores ($r_s = -0.21$; 95% CI: −0.40, −0.0054; $p = 0.039$). Higher 5-year weed pollen exposure correlated with worse SNOT-22 scores ($r_s = 0.20$; 95% CI: 0.00054, 0.38; $p = 0.043$).

Conclusion: This multi-institutional pilot study suggests that weed and ragweed pollen may negatively impact the QOL of patients with CRS, but further studies are needed to confirm these findings.

Level of Evidence: 3.

Trial Registration: Clinical trial registration ID: NCT02720653 (www.clinicaltrials.gov)

1 | Introduction

Pollen is a ubiquitous aeroallergen that primarily effects sensitized individuals through IgE and T helper type 2 immune responses [1]. These responses lead to local and systematic effects that are commonly associated with allergic pathology such as rhinoconjunctivitis, postnasal drip, cough, nasal congestion, nasal obstruction, and fatigue [1]. Because of the importance and prevalence of airborne pollen, the American Academy of Allergy, Asthma and Immunology (AAAAI) created a program to measure pollen spores to facilitate research on the impact pollen exposure plays in populations [2, 3].

Chronic rhinosinusitis (CRS) is a disease distinguished by inappropriate inflammation of the nasal and paranasal mucosa leading to symptoms of nasal obstruction, nasal discharge, facial pain or pressure, and olfactory dysfunction [4–6]. Environmental factors, such as airborne irritants, may play an important role in the pathophysiology of chronic rhinosinusitis (CRS) [7]. Nevertheless, the relationship between pollen and CRS is understudied [8, 9], and no studies to date have examined the role of aerosolized pollen exposure at presentation on CRS disease severity and patient-reported outcome measures. This pilot study seeks to tackle this knowledge gap by examining the association between long-term pollen exposure and sinonasal-specific, as well as general, quality-of-life measures.

2 | Methods

2.1 | Study Design and Sample Population

In a single-arm, multi-center, longitudinal outcomes study design, participants were enrolled prospectively across four academic medical centers: Oregon Health & Science University (Portland, OR), the Medical University of South Carolina (Charleston, SC), the University of Colorado (Aurora, CO), and the University of Utah School (Salt Lake City, UT). Study and clinical data safety protocols were approved by the individual Institutional Review Boards of each institution, and written informed consent was provided by each study participant.

2.2 | Inclusion Criteria

Adult patients (> 18 years of age) diagnosed with CRS by a rhinologist in accordance with the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) criteria [10] were included. Patients with cystic fibrosis, primary ciliary dyskinesia, sinonasal tumors, odontogenic sinusitis, immunodeficiency, current immunomodulator therapy, as well as those considered vulnerable populations were excluded.

2.3 | Environmental Pollen Determination

Pollen data was obtained through the National Allergy Bureau (NAB) from counties in Oregon, South Carolina, Colorado, and Utah. Pollen sampling was conducted in accordance with the standard procedures of the NAB [2]. Pollen exposure was divided into weed, ragweed and grass pollen [11]. This breakdown was chosen a priori, and all participant's home addresses resided with a county of a measurement station. Mean annual pollen exposure over a 5-year period before enrollment was calculated for each participant and noted to represent their pollen exposure.

2.4 | Clinical Measures of Disease Severity

The 22-item SinoNasal Outcomes Test (SNOT-22; 2006; Washington University, St. Louis, MO) survey scores [12] and SF-6D health utility value (HUV) scores [13] were calculated from survey results obtained at the time of enrollment. The SF-6D score represents a standardized value reflecting how an individual patient rates their specific health state. Health utility values range from 0.3 to 1.0, with lower scores indicating a poorer perceived health state and a score of 1.0 indicating perfect health. Atopy status was assigned by participants designating on a questionnaire that they had a history of positive allergy testing.

2.5 | Biostatistical Analyses and Data Management

Participant data was inputted in a central database (Access; Microsoft Corporation; Redmond, WA) and all protected health information was removed, and unique identification numbers were assigned before data transfer. GraphPad Prism 9.5.1 (GraphPad Software; San Diego, CA) was used for data analysis. Data normality was assessed using Normal Q–Q plots and Shapiro–Wilk testing. Descriptive characteristics are represented using means, standard deviation [±SD] values, and range limits. Two-tailed, bivariate Spearman's rank correlation coefficients (r_s) were used in conjunction with Bonett and Wright 95% confidence intervals (CIs) to explore associations.

3 | Results

3.1 | Descriptive Statistics

A total of 103 patients were included in this study with a median age of 48.6 [±14.6] years. Females comprised 42.7% of participants while 57.3% were male. Nasal polyps were present in 48 (46.6%) patients and 57 (55.3%) had a history of atopy designated by patient-reported history of positive allergy testing (Table 1). Eight (7.8%) patients had AERD and 48 (46.6%) had previous sinus surgery (Table 1).

3.2 | Pollen Exposure Correlates With Increased Disease-Specific and General QOL Severity

Higher 5-year mean ragweed pollen exposure correlated with worse presenting SNOT-22 ($r_s = 0.24$; 95% CI: 0.033, 0.42; $p = 0.019$) and SF-6D scores ($r_s = -0.21$; 95% CI: −0.40, −0.0054; $p = 0.039$). Higher 5-year weed pollen exposure correlated with worse SNOT-22 scores ($r_s = 0.20$; 95% CI: 0.00054, 0.38; $p = 0.043$). Weed pollen exposure did not significantly correlate with SF-6D scores ($r_s = -0.15$; 95% CI: −0.34, 0.054; $p = 0.14$; Table 2). Univariate analysis was performed for covariables

TABLE 1 | Descriptive characteristics of final cohort.

Characteristic/cofactors (*n*)	Mean [±SD]	Range: LL, UL	*n* (%)
Age (years)	48.6 [±14.6]	19, 76	—
Males	—	—	59 (57.3)
Females	—	—	44 (42.7)
White/Caucasian	—	—	98 (95.1)
Non-White/Caucasian	—	—	5 (4.9)
Hispanic/Latino	—	—	4 (3.9)
Non-Hispanic Latino	—	—	99 (96.1)
Household income	—	—	—
$0–$25,000	—	—	7 (6.8)
$26,000–$50,000	—	—	11 (10.7)
$51,000–$75,000	—	—	13 (12.6)
$76,000–$100,000	—	—	28 (27.2)
$100,000+	—	—	24 (23.3)
Unknown/unwilling to report	—	—	20 (19.4)
Nasal polyposis	—	—	48 (46.6)
Septal deviation	—	—	31 (30.1)
Previous sinus surgery	—	—	48 (46.6)
Acetylsalicylic acid sensitivity/AERD	—	—	8 (7.8)
GERD	—	—	27 (26.2)
Atopy	—	—	57 (55.3)
Lund-Kennedy endoscopy score (103)	5.9 [±3.7]	1.0, 20.0	—
Lund-Mackay CT score (100)	13.2 [±5.8]	1.0, 24.0	—
SNOT-22 total score (103)	51.0 [±21.0]	3.0, 102.0	—
SF-6D HUV score (102)	0.66 [±0.23]	0.00, 1.00	—

Note: Descriptive characteristics of final study cohort population ($n = 103$).
Abbreviations: AERD, aspirin exacerbated respiratory disease; CAMT, continued appropriate medical therapy; CT, computed tomography; ESS, endoscopic sinus surgery; GERD, gastroesophageal reflux disease; HUV, health utility value; LL, lower limit; *N*, sample size; SD, standard deviation; SF-6D, Medical Outcomes Study Short-Form 6-D; SNOT-22, 22-item Sinonasal Outcome Test; UL, upper limit.

listed in Table 1 and no significant associations were found ($p > 0.050$); given that no other independent significant associations were identified for covariables listed in Table 1 on this univariate model screening, multivariate analysis was precluded.

4 | Discussion

Aeroallergens increase the infiltration of inflammatory cells and mediators in the nasal and paranasal mucosa in sensitized patients [14, 15]. Patients become sensitized when pollen penetrating the mucosa interact with T cells leading to B cell activation [15, 16]. B cells then produce IgE which activates an allergic response on re-exposure through mast cell and basophil activity [15, 17]. In settings of chronic exposure, the infiltration of inflammatory cells, and their related inflammatory mediators, can disrupt the epithelial barrier which can lead to mucosal hypertrophy and hypersensitivity [14, 16]. Despite the effect of pollen on mucosal physiology, studies investigating the link between allergy and CRS have mixed results, with systematic reviews unable to draw concrete conclusions regarding the role of allergy in CRS [8, 9]. The lack of definitive conclusions may be partially attributable to the heterogeneity of CRS pathophysiology, which can exhibit several different endotypes [7]. Furthermore, as AR and CRS are often comorbid, it can be difficult to tease out independent relationships.

The present study is the first to investigate the association between long-term pollen exposure and SNOT-22 and SF-6D scores in patients with CRS. Our data indicate that mean 5-year weed and ragweed pollen exposure is associated with worse SNOT-22 scores, while ragweed pollen exposure is additionally associated with poorer SF-6D scores. A previous study examining the relationship between pollen exposure and AR demonstrated that only weed and tree pollen increased the incidence of medication fills for AR, while other sources of pollen did not [11].

TABLE 2 | Bivariate associations between 5-year pollen exposure and disease severity.

	N	R_s	CI	p
Ragweed pollen				
SNOT-22	97	0.2370	0.03341, 0.4216	0.0194
SF-6D	96	−0.2407	−0.4258, −0.03627	0.0182
Weed pollen				
SNOT-22	103	0.1996	0.0005378, 0.3835	0.0432
SF-6D	101	−0.1489	−0.3398, 0.05382	0.1374
Grass pollen				
SNOT-22	103	0.07255	−0.1274, 0.2668	0.4643
SF-6D	102	−0.005223	−0.2051, 0.1951	0.9585

Note: R_s, Spearman's rank correlation coefficient.
Abbreviations: CI, 95% confidence interval; *N*, number of participants; SF-6D, Medical Outcomes Study Short-Form 6-D; SNOT-22, 22-item Sinonasal Outcome Test.

Our investigation adds to the evidence that weed pollen may be uniquely impactful on upper airway inflammatory disease.

The participant sample size in our study is small, as the number of counties with a NAB-sponsored measurement station is few. Further research with a larger sample size should be considered to fully elucidate the clinical relevance of the association noted in our work. Additionally, our cohort included only patients who sought care at academic medical centers, thus potentially limiting generalizability. SNOT-22 and SF-6D surveys were only collected at enrollment which may represent a less accurate prediction of disease severity, and we cannot confirm that participants resided continuously in their zip code for 5 years. Finally, MV modeling was not warranted in our dataset, but future studies could consider sources of unmeasured confounding.

Ultimately, this multi-institutional pilot study sampling multiple geographic locations suggests that weed and ragweed pollen exposure may negatively impact the QOL of patients with CRS, but further studies are needed to confirm these findings.

Conflicts of Interest

D.M.B.: Grant support from NIH/NHLBI, CF Foundation, International Society of Inflammation and Allergy of the Nose and the American Rhinologic Society CORE/Sue Ann and John L. Weinberg Foundation unrelated to this work; honoraria from sources including National Jewish Health; consulting fees from Amgen, on medicolegal cases and from Garner Health (equity). J.A.A: GlycoMira consultant, equity. GSK advisory board, speaker panel. Sanofi advisory board consultant, OptiNose consultant, Medtronic consultant. Z.M.S.: Lyra, Optinose, Regeneron consultant. Medical director Healthy Humming. S.B. Grant support from NIH/NIEHS/NIOSH, NINDS, State of Michigan. V.R.R.: Grant support from NIH/NIAID; Medtronic Inc, consultant. A.S.G.: Grant support from NIH/NIEHS.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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